Published in final edited form as:
Diabetes Care. 2008 March ; 31(3): 525–527.

FreeStyle Navigator™ Continuous Glucose Monitoring System Use in Children with Type 1 Diabetes using glargine-based multiple daily dose regimens: Results of a Pilot Trial

Diabetes Research in Children Network (DirecNet) Study Group

Abstract

In a previous pilot study of the FreeStyle Navigator™ Continuous Glucose Monitoring System ("Navigator", Abbott Diabetes Care) in 30 children and adolescents with type 1 diabetes (T1D) using insulin pumps, we found that Navigator use averaged >130 hours per week over 13 weeks and mean HbA1c dropped from 7.1 ± 0.6% to 6.8 ± 0.7% (p=0.02) (1). The current study evaluated whether the Navigator was similarly tolerated over 13 weeks in 27 children aged 4–17 years with T1D using glargine-based multiple daily injection (MDI) insulin regimens. Subjects averaged >100 hours/week of Navigator use. Mean HbA1c fell from 7.9 ± 1.0% at baseline to 7.3 ± 0.9% at 13 weeks (p=0.004). High satisfaction with the Navigator was reported on the Continuous Glucose Monitor Satisfaction Scale. These encouraging pilot study results support the inclusion of MDI users in longer-term randomized clinical trials of continuous glucose monitors (CGM).

Keywords

Real-time glucose monitoring; Childhood Diabetes and Childhood Type 1

Research Design and Methods

Institutional Review Boards at each of the DirecNet centers approved the study protocol and consent/assent forms. Methods were virtually identical to those employed in our previous Navigator study (1), except that all subjects were treated with glargine-based MDI treatment. Other eligibility requirements were: 1) age 3-<18 years, 2) T1D ≥1 year duration, 3) home computer with e-mail access and 4) parent/older subject comprehended English. Subjects were excluded for: 1) asthma, 2) cystic fibrosis, 3) psychiatric disorder and 4) use of glucocorticoids. Subjects were selected for participation from the existing patient population at each center.

There was a run-in period of one week during which Navigator use was blinded to collect baseline glucose data followed by unblinded home use of the Navigator for 3 months. To blind subjects to the results from the Navigator sensor readings, Abbott Diabetes Care provided software which modified the display on the receiver so that the sensor readings would not display but results of FreeStyle glucose testing would be displayed. During this run-in subjects were required to perform at least 4 glucose tests daily. Five of the 32 subjects withdrew during the run-in phase because of difficulty using the sensor or other problems. The remaining 27

Corresponding Author: Stuart Weinzimer, MD, c/o DirecNet Coordinating Center, Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647. Phone: 813-975-8690. Fax: 813-903-8227. E-mail: direcnet@jaeb.org.

subjects were asked to use the Navigator continuously and instructed on how to use the sensor data to make management decisions (2). Subjects downloaded the Navigator weekly and transmitted the data to the clinical and coordinating centers. Patients were seen at 3, 7 and 13 weeks and called at 0.5, 2, 4, 8 and 10 weeks to review glucose data and adjust treatment. A1c was measured with the DCA 2000® + (Bayer, Inc.). Parents and subjects ≥9 years of age completed the PedsQL Diabetes Module (3), Fear of Hypoglycemia Survey (4,5) and the Continuous Glucose Monitor Satisfaction Scale (6).

Glycemic indices were calculated giving equal weight to each of the 24 hours of the day. Standard deviation (SD), mean amplitude of glycemic excursions (MAGE) (7) and mean absolute rate of change (8) were calculated. Paired t-tests were used to compare baseline with 9–13 week data.

Results

The mean ± SD age of the 27 subjects was 11.0 ± 3.9 years (range 4–17), median (quartiles) duration of diabetes was 3.4 (2.0, 5.2) years, and mean ± SD HbA1c was 7.9 ± 1.0%. HbA1c was ≤7.5% in 10 and >7.5% in 17 subjects. Four subjects dropped out before the 13-week visit and the remaining 23 completed the 13-week study. As shown in the Table, subjects averaged over 100 hours of sensor wear per week, and the frequency of sensor use did not change significantly after the run-in phase. A similar trend was observed in meter measurements.

Mean HbA1c fell from 7.9 ± 1.0% at baseline to 7.3 ± 0.9% at 13 week (p=0.004) with the greatest reduction being when baseline A1c was >7.5%. Mean glucose concentration dropped early (baseline vs. weeks 1–4: p=0.002) but no further drop occurred during weeks 9–13. There was a similar trend for the percentage of glucose values in the target range of 71–180 mg/dL (p=0.004). Glycemic variation decreased (baseline vs. weeks 9–13: p=0.001 for MAGE) and there were no severe hypoglycemia events during the study. There was no association between number of meter tests per day and HbA1c.

Subjects and parents reported high overall satisfaction with the Navigator on the Continuous Glucose Monitor Satisfaction Scale (CGM-SAT) with average item scores of 3.5 ± 0.5 for subjects and 3.8 ± 0.4 for parents on a 5-point Likert scale where 3.0 is a neutral score. Fear of Hypoglycemia Survey and PedsQL scores did not change, although on the CGM-SAT at 13 weeks subjects and parents both agreed that the sensor “makes me feel safer knowing that I will be warned about low blood sugar before it happens” (mean 3.9 and 4.5 for subjects and parents, respectively)./.

Conclusions

In this pilot study we assessed whether continuous glucose monitoring could be utilized consistently and effectively in youth with T1D on glargine-based MDI therapy. We found that: 1) the majority of subjects used the Navigator on an almost daily basis, 2) parents and patients were very satisfied with the device, and 3) indices of glycemic control improved. Additionally, all 23 subjects who completed the 13-week visit elected to continue to use the Navigator during an optional continuation phase. Improvements in glycemic control were seen shortly after initiation of continuous glucose monitoring and were sustained for the duration of the study.

The Navigator provided a safe and effective complement to standard glucose meter monitoring even though none of the subjects in this study had used insulin pump therapy and none had prior experience with the use of an external, transcutaneous device. Although these subjects were not strictly comparable to pump patients in our prior Navigator study (e.g., baseline A1c levels were higher in the MDI subjects), major outcomes were similar in these MDI-treated patients. Moreover, the findings from both of the DirecNet Navigator pilot studies are in

marked contrast to the results of our study of the GlucoWatch (9), a device that children and adolescents with T1D found too difficult to use consistently.

While our results are encouraging, they must be viewed cautiously since there was no concurrent control group and follow-up only lasted 3 months. Nevertheless, these preliminary data support the inclusion of MDI patients in longer-term randomized clinical trials evaluating the effectiveness of CGM use in children with T1D.

Acknowledgements

This research was supported by the following NIH/NICHD Grants: HD041919-01; HD041915-01; HD041890; HD041918-01; HD041908-01; and HD041906-01. Clinical Centers also received funding through the following GCRC Grant Numbers M01 RR00069; RR00059; RR 06022 and RR00070-41. Abbott Diabetes Care, Alameda, CA, provided the FreeStyle Navigator™ Continuous Glucose Monitoring Systems and the FreeStyle Blood Glucose Meter test strips.

References

1. Diabetes Research in Children Network (DirecNet) Study Group. Continuous Glucose Monitoring in Children with Type 1 Diabetes. The Journal of Pediatrics 2007;151:388–393. [PubMed: 17889075]
2. Diabetes Research in Children Network (DirecNet) Study Group. Use of the DirecNet Applied Treatment Algorithm (DATA) for diabetes management with a real-time continuous glucose monitor (the Freestyle Navigator). Pediatric Diabetes. In press
3. Varni JW, Burwinkle TM, Jacobs JR, Gottschalk M, Kaufman F, Jones KL. The PedsQL™ in Type 1 and Type 2 diabetes: reliability and validity of the Pediatric Quality of Life Inventory™ Generic Core Scales and Type 1 Diabetes Module. Diabetes Care 2003;26:631–637. [PubMed: 12610013]
4. Clarke WL, Gonder-Frederick LA, Snyder AL, Cox DJ. Maternal fear of hypoglycemia in their children with insulin-dependent diabetes mellitus. J Pediatr Endocrinol Metab 1998;11:189–194. [PubMed: 9642659]
5. Green LB, Wysocki T, Reineck BM. Fear of hypoglycemia in children and adolescents with diabetes. J Pediatr Psychol 1990;15:633–641. [PubMed: 2283572]
6. Diabetes Research in Children Network (DirecNet) Study Group. Youth and parent satisfaction with clinical use of the Glucowatch G2 Biographer in the management of pediatric type 1 diabetes. Diabetes Care 2005;28:1929–1935. [PubMed: 16043734]
7. Service FJ, Molnar GD, Rosevear JW, Ackerman E, Gatewood LC, Taylor WF. Mean amplitude of glycemic excursions, a measure of diabetic instability. Diabetes 1970;19:644–655. [PubMed: 5469118]
8. Kovatchev BP, Clarke WL, Breton M, Brayman K, McCall A. Quantifying temporal glucose variability in diabetes via continuous glucose monitoring: mathematical methods and clinical application. Diabetes Technol Ther 2005;7:849–862. [PubMed: 16386091]
9. Diabetes Research in Children Network (DirecNet) Study Group. A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes. Diabetes Care 2005;28:1101–1106. [PubMed: 15855573]

Appendix

Writing Committee

Stuart Weinzimer, MD; Dongyuan Xing, MPH; Michael Tansey, MD; Rosanna Fiallo-Scharer, MD; Nelly Mauras, MD; Tim Wysocki, PhD; Roy Beck, MD, PhD; William Tamborlane, MD; Katrina Ruedy, MSPH; and the Diabetes Research in Children Network (DirecNet) Study Group

The DirecNet Study Group

Clinical Centers: (Listed in alphabetical order with clinical center name, city, and state. Personnel are listed as (PI) for Principal Investigator, (I) for co-Investigator and (C) for Coordinators.) (1) **Barbara Davis Center for Childhood Diabetes, University of Colorado, Denver, CO:** H. Peter Chase, MD (PI); Rosanna Fiallo-Scharer, MD (I); Laurel Messer, RN (C); Barbara Tallant, RN, MA (C); Victoria Gage, RN (C); (2) **Department of Pediatrics, University of Iowa Carver College of Medicine, Iowa City, IA:** Eva Tsalikian, MD (PI); Michael J. Tansey, MD (I); Linda F. Larson, RN (C); Julie Coffey, MSN (C); Joanne Cabbage (C); (3) **Nemours Children's Clinic, Jacksonville, FL:** Tim Wysocki, PhD, ABPP (PI); Nelly Mauras, MD (I); Larry A. Fox, MD (I); Keisha Bird, MSN (C); Kim Englert, RN (C); (4) **Division of Pediatric Endocrinology and Diabetes, Stanford University, Stanford, CA:** Bruce A. Buckingham, MD (PI); Darrell M. Wilson, MD (I); Paula Clinton, RD, CDE (C); Kimberly Caswell, APRN; (**5) Department of Pediatrics, Yale University School of Medicine, New Haven, CT:** Stuart A. Weinzimer, MD (PI); William V. Tamborlane, MD (I); Elizabeth A. Doyle, MSN (C); Heather Mokotoff, MSN (C); Amy Steffen (C); Brett Ives, ARNP (C); **Coordinating Center: Jaeb Center for Health Research, Tampa, FL:** Roy W. Beck, MD, PhD; Katrina J. Ruedy, MSPH; Craig Kollman, PhD; Dongyuan Xing, MPH; Cynthia R. Stockdale; Judy Jackson; **University of Minnesota Central Laboratory:** Michael W. Steffes, MD, PhD; Jean M. Bucksa, CLS; Maren L. Nowicki, CLS; Carol A. Van Hale, CLS; Vicky Makky, CLS; **National Institutes of Health:** Gilman D. Grave, MD; Mary Horlick, PhD; Karen Teff, PhD; Karen K. Winer, MD; **Data and Safety Monitoring Board:** Dorothy M. Becker, MBBCh; Patricia Cleary, MS; Christopher M. Ryan, PhD; Neil H. White, MD, CDE; Perrin C. White, MD

Table

Major Outcomes Summary Table (*mean ± SD or %)*

	Baseline	Weeks 1–4	Weeks 5–8	Weeks 9–13	P-Value baseline vs. wks 9–13	P-Value wks 1–4 vs. wks 9–13
	N=27	N=27	N=25*	N=23*		N=23
Navigator Use per week						
Hours of wear	153 ± 30	107 ± 52	114 ± 50	107 ± 44	N/A	0.25
Hours of glucose readings	99 ± 42	79 ± 42	79 ± 41	77 ± 41	N/A	0.12
Meter Tests per day	4.9 ± 1.4	3.2 ± 1.7	2.9 ± 1.7	2.6 ± 1.6	N/A	0.16
	N=27		N=24	N=23	N=23	
HbA1c (%)						
All subjects	7.9 ± 1.0	N/A	7.4 ± 0.8	7.3 ± 0.9	0.004	N/A
Baseline ≤ 7.5%	7.0 ± 0.5	N/A	6.7 ± 0.6	6.6 ± 0.5	0.03	N/A
Baseline > 7.5%	8.5 ± 0.7	N/A	7.8 ± 0.6	7.8 ± 0.7	0.02	N/A
	N=26†	N=26†	N=23†	N=23	N=22‡	N=23‡
Mean Glucose (mg/dL)						
All subjects	191 ± 34	172 ± 18	171 ± 23	181 ± 31	0.25	0.05
Baseline ≤ 7.5%	170 ± 28	162 ± 21	161 ± 23	159 ± 22	0.38	0.98
Baseline > 7.5%	205 ± 31	179 ± 13	177 ± 22	196 ± 29	0.49	0.03
% Values 71–180 mg/dL						
All subjects	46%	55%	55%	50%	0.32	0.04
Baseline ≤7.5%	56%	62%	61%	62%	0.36	0.54
Baseline > 7.5%	40%	51%	52%	42%	0.68	0.06
Hypoglycemia						
% values ≤70 mg/dL	4.4%	3.3%	4.0%	3.4%	0.36	0.75
% values ≤60 mg/dL	2.6%	1.6%	1.9%	1.6%	0.27	0.63
% values ≤50 mg/dL	1.39%	0.76%	0.93%	0.79%	0.30	0.52
% values ≤40 mg/dL	0.85%	0.40%	0.57%	0.42%	0.33	0.36
Hypoglycemia Area§	0.75	0.43	0.54	0.44	0.25	0.60
Hyperglycemia						
% values >180 mg/dL	50%	42%	41%	47%	0.54	0.07
% values >200 mg/dL	42%	33%	32%	38%	0.45	0.06
% values >250 mg/dL	25%	14%	15%	19%	0.12	0.01
% values >300 mg/dL	11.2%	4.5%	5.0%	7.3%	0.07	0.008
Hyperglycemia Area‖	40	25	26	32	0.17	0.02
Glucose Lability						
SD *(mg/dL)*	74	67	67	69	0.12	0.04
MAGE *(mg/dL)*	147	128	126	127	0.001	0.66
Mean absolute rate of change#	0.84	0.81	0.77	0.79	0.16	0.44

*Three subjects dropped prior to 7-week visit and another dropped prior to 13-week visit; one had baseline A1c ≤7.5% and 3 had baseline A1c >7.5%.

†Subjects with less than 24 hours of Navigator glucose readings were excluded from calculation of glycemic indices.

‡Number of subjects with at least 24 hours of Navigator glucose readings for both time points.

§Total area below 70 mg/dL; reflects both percentage and severity of glucose values in the hypoglycemic range.

‖Total area above 180 mg/dL; reflects both percentage and severity of glucose values in the hyperglycemic range.

[#] Rate of change calculated using consecutive Navigator readings 10 minutes apart (mg/dL/min).